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Review Article

Esophageal Impedance: Role in the Evaluation of Esophageal Motility

Chien-Lin Chen*

Department of Medicine, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

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Abstract

The esophagus is a hollow muscular tube with ends closed proximally and distally by muscular sphincters. The upper esophageal sphincter and proximal one third of the esophageal body are composed of striated muscle. There is then a transition zone where striated and smooth muscle mix together. The lower esophageal sphincter and the distal one half to two thirds of the esophageal body are composed of smooth muscle. Esophageal peristalsis results from sequential contraction of circular muscles, which serves to push the ingested food bolus toward the stomach with minimal stasis in the esophageal body. Therefore, esophageal motility testing aims to investigate esophageal function and to reveal any disorders to explain individual symptoms and provide a rationale for treatment. In 1991, impedance monitoring was introduced by Jiri Silny as a new technique to detect the flow of certain physical properties through hollow viscera, which later inspired numerous studies in which the possible applications of this technique were investigated. When combined with manometry, impedance provides information on esophageal bolus transit while manometry provides information on esophageal contractile activity. Subsequently, normal values for combined impedance and manometry have been reported with different methodologies worldwide, and such technique allows the acquisition of more information than manometry alone in patients with esophageal motility abnormalities. Therefore, combined impedance and manometry is emerging as an important tool for understanding and obtaining detailed information about the physiology and pathophysiology relevant to esophageal motility. Other potential clinical implications of this technique may include the functional classification of esophageal motor disturbances in patients with non-obstructive dysphagia, and the perioperative management of laparoscopic fundoplication which could impact esophageal motility. In this review, the clinical applications of this emerging new technique are summarized with regard to the technical aspects of this technology. The advantages they offer over conventional techniques for the evaluation of esophageal motor diseases are reported. (*Tzu Chi Med J* 2009;21(2):110–117)

*Corresponding author. Department of Medicine, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung-Yang Road, Hualien, Taiwan.
E-mail address: harry.clchen@msa.hinet.net

1. Introduction

From mouth to stomach, the food conduit includes the oral cavity, pharynx, and esophagus. The esophagus functions as a dynamic tube, pushing food toward the stomach, where digestion and absorption can take place. Mucus produced by the esophageal mucosa provides lubrication and eases the passage of food. Active peristaltic contractions, i.e., primary peristalsis, propel residual material from the esophagus into the stomach. During vomiting and reflux, the esophagus also serves as a passageway for gastrointestinal contents traveling retrograde from the stomach or small intestine.

In 1991, impedance monitoring was introduced by Jiri Silny as a new technique to detect the flow of liquids and gas through hollow viscera (1). Silny's landmark publication triggered various studies in which possible applications of this technique were investigated. Subsequently, it has now become apparent that impedance monitoring offers new opportunities in the field of esophageal transit testing and gastroesophageal reflux monitoring.

The impedance technique alone cannot measure contraction amplitude and other important parameters of esophageal function, which may limit some observations of the relationships between esophageal wall movement and bolus motion, especially in patients with suspected esophageal motor disorder or dysphagia. Therefore, the catheter integrating impedance monitoring and manometry in a single device has been developed. Both tests can be performed simultaneously and the relationship between the dynamics of bolus transport and wall motion can be evaluated

well, while the quality of the recording is maintained. In this review, we will focus on the clinical applications of this emerging new technique and summarize current results.

2. Principles and scientific basis

The method is based on the esophageal intraluminal measurement of electrical impedance and pressure between a number of arranged electrodes and pressure sensors during a bolus transit using an intraluminal probe (Fig. 1) (2). The electrical impedance is inversely proportional to the electrical conductivity of the luminal contents and the cross-sectional area (Fig. 1) (2). Saliva or nutrients show a higher conductivity and therefore induce an impedance drop at the corresponding measurement segments, whereas air has a lower electrical conductivity and yields increased impedance. On the other hand, luminal dilatation results in an impedance drop, whereas luminal narrowing causes an increase in impedance (1).

The bolus passage along each measured segment allows the alteration of the typical tracing of impedance, which includes a maximum of five phases (Fig. 2, upper panel): (1) phase 1 is the resting stage of the organ; (2) phase 2 represents the facultative arrival and passage of an air volume ahead of the bolus; (3) phase 3 is associated with the arrival and the passage of a bolus. The initial rapid fall of impedance is associated with the arrival of the bolus front as bolus entry (F-Point). During the subsequent nearly plateau phase, the bolus is mainly located within the measuring segment; the minimum impedance

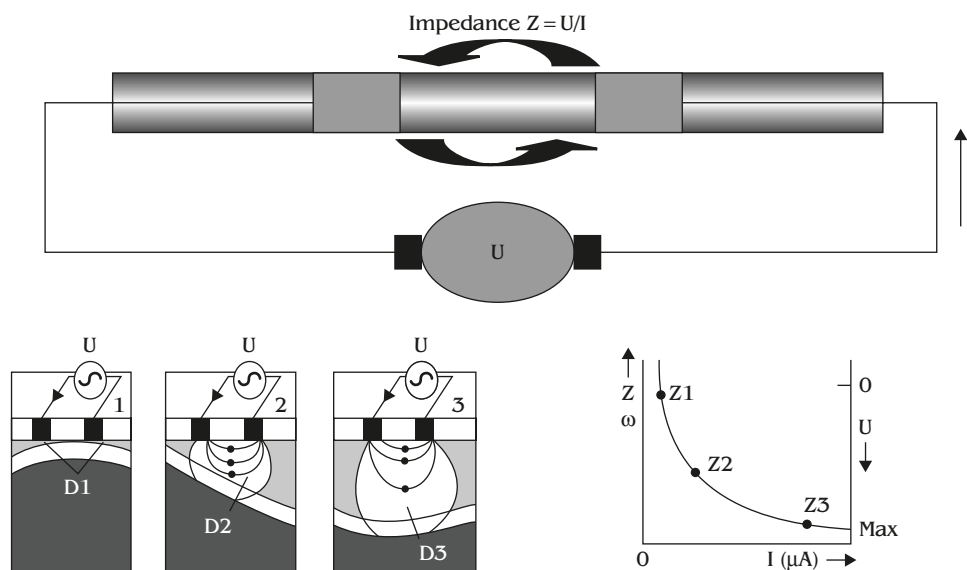


Fig. 1 — Upper: electrical impedance (Z) of an electric field between two electrodes is the ratio between applied voltage (U) and resulting current (I). Lower: impedance is non-linearly inversely dependent on bolus diameter and electrical conductivity of luminal content (2).

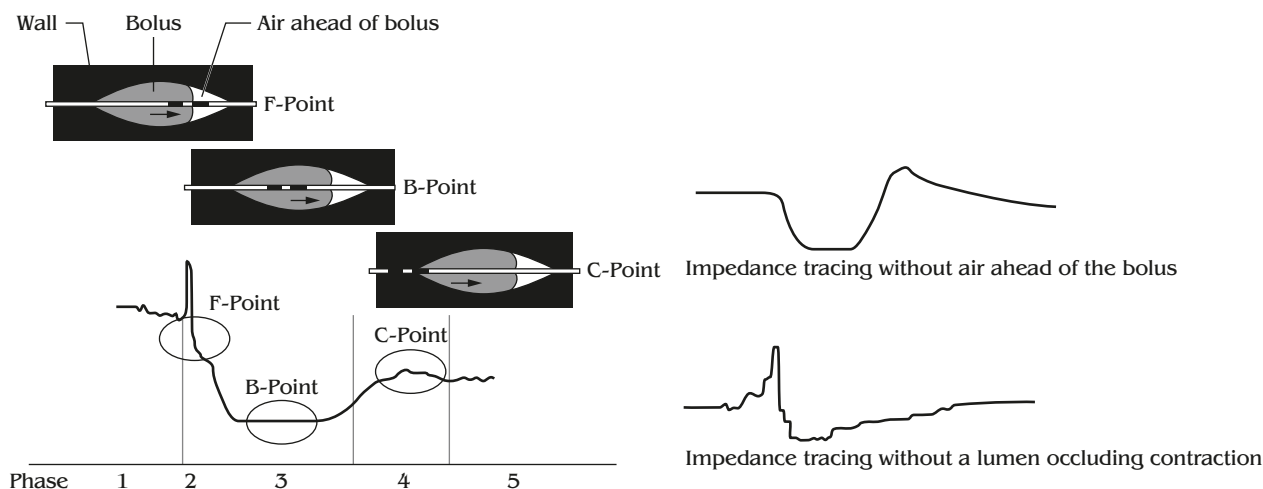


Fig. 2 — Characteristics of the impedance tracing during bolus passage in the esophagus of healthy persons [2].

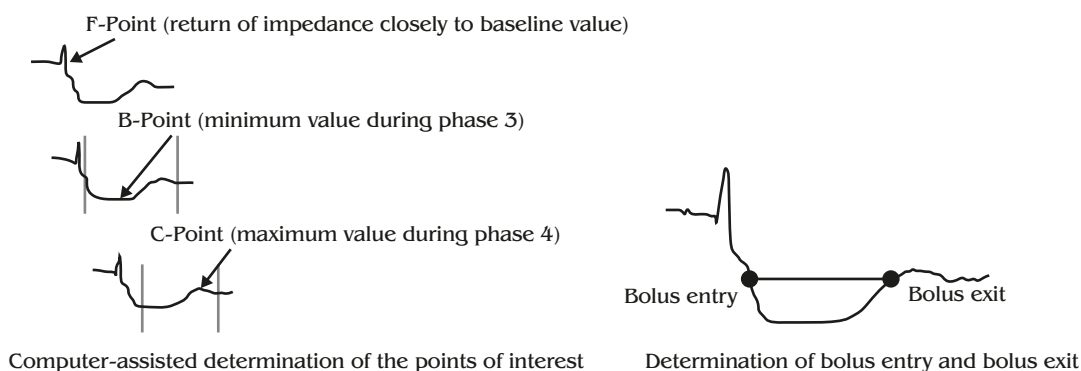


Fig. 3 — Left: computer-assisted determination of the points of interest according to presumed definitions [3]. Right: bolus entry and bolus exit can be considered to be 50% of the basal impedance as compared to nadir impedance as suggested by Tutuian et al [4].

during this phase represents the bolus body (B-Point); (4) during phase 4, the bolus leaves the measuring segment as bolus exit due to wall contraction with facultative lumen occlusion, which can be represented by the maximum impedance (C-Point); (5) phase 5 is the transitory stage to resting stage. This characteristic impedance wave form may change in the case of absence of air in front of the bolus or absence of a lumen-occluding contraction wave (Fig. 2, upper panel). For visualization of the maximum and minimum impedance values, an individual scaling (Fig. 2, lower panel, left side) can be used instead of the standard scaling (Fig. 2, lower panel, right side) [2].

The F-Point, B-Point and C-Point can be determined according to the resumed definitions, as shown in Fig. 3, left panel [3,4]. Alternatively, bolus entry and exit have been defined as follows [5]: bolus entry is considered to occur at the 50% point between the impedance baseline and the impedance nadir during bolus passage, and bolus exit is determined as the

50% point on the impedance recovery curve, as shown in Fig. 3, right panel [3,4].

3. Equipment and technique

Fisher et al first described the technique for measuring intraluminal impedance in 1978 [6]. An intraluminal probe is used to measure the electrical impedance between closely arranged electrodes during a bolus passage. Cylindrical metal electrodes are mounted along the length of a thin plastic catheter, which is passed through the nose into the esophagus (Fig. 4) [7,8]. The impedance could be designed to integrate with either pH sensors (impedance-Ph) or manometry (combined impedance and manometry).

Each neighboring pair of electrodes (known as an impedance segment or impedance channel) is connected to an impedance voltage transducer, which delivers a measuring current. The measurement

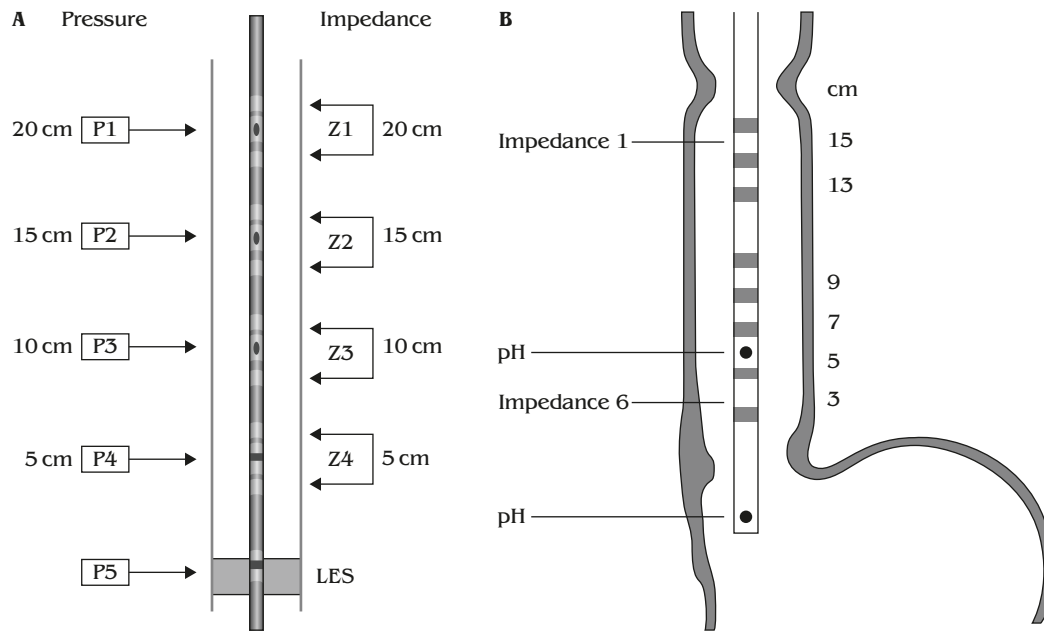


Fig. 4 — (A) Nine-channel combined impedance and manometry catheter; (B) combined impedance-pH catheter consisting of six impedance channels and two pH sensors [7]. Circumferential solid-state pressure sensors located in the lower esophageal sphincter (LES) high-pressure zone (P5) and 5 cm above it (P4); unidirectional solid state pressure sensors located 10 cm (P3), 15 cm (P2), and 20 cm (P1) above the LES. Impedance-measuring segments centered 5 cm (Z4), 10 cm (Z3), 15 cm (Z2), and 20 cm (Z1) above the LES [8].

represents the electrical impedance around the catheter in the section between each pair of electrodes. The impedance is inversely proportional to the electrical conductivity of the luminal contents and the cross-sectional area between the two electrodes. Air has a low conductivity and, therefore, yields an impedance increase, whereas swallowed or refluxed material has a high conductivity and yields an impedance decrease. Furthermore, luminal dilation (i.e., induced by bolus entry in the measuring segment) results in an impedance decrease, whereas luminal narrowing (i.e., during an occlusive contraction) causes an impedance increase [9]. Changes in the temporal-spatial patterns in impedance are thus identified at various levels within the esophagus, allowing differentiation between antegrade (swallow) and retrograde (reflux) bolus movement [10].

4. Physiological observation of esophageal transport

4.1. Validation studies

During esophageal manometry, intraluminal pressure sensors (either water perfused or solid state) are used to record the pressures generated within the esophageal body and the resting and residual lower esophageal sphincter (LES) pressure during standardized swallows. Manometry offers information on the

amplitude and peristaltic progression of the esophageal contractions but provides only limited information on the bolus transit [11]. Early studies combining manometry and videofluoroscopy have determined that esophageal contractions with an amplitude greater than 30 mmHg are accompanied by complete bolus transit (CBT) [12]. Combined impedance monitoring and manometry is able to offer information on both esophageal pressure and bolus transit without the use of radiation (Fig. 5) [13,14].

The accuracy of impedance to determine bolus transit was validated by studies combining impedance monitoring and videofluoroscopy. A study in healthy volunteers by Simren et al found a good correlation between videofluoroscopy and impedance measurements to estimate the time to esophageal filling ($r^2=0.89$; $p<0.0001$) and time to esophageal emptying ($r^2=0.79$; $p<0.0001$) [15]. More recently, Imam et al reported on the correlation between bolus transit parameters as assessed by impedance measurements and fluoroscopy in 13 healthy volunteers, indicating that the two techniques yielded concordant results in 97% (72/74) of swallows [16].

4.2. Normal data for esophageal bolus transit

Esophageal function testing using combined impedance-manometry in healthy volunteers has been reported by several groups. It is mostly performed

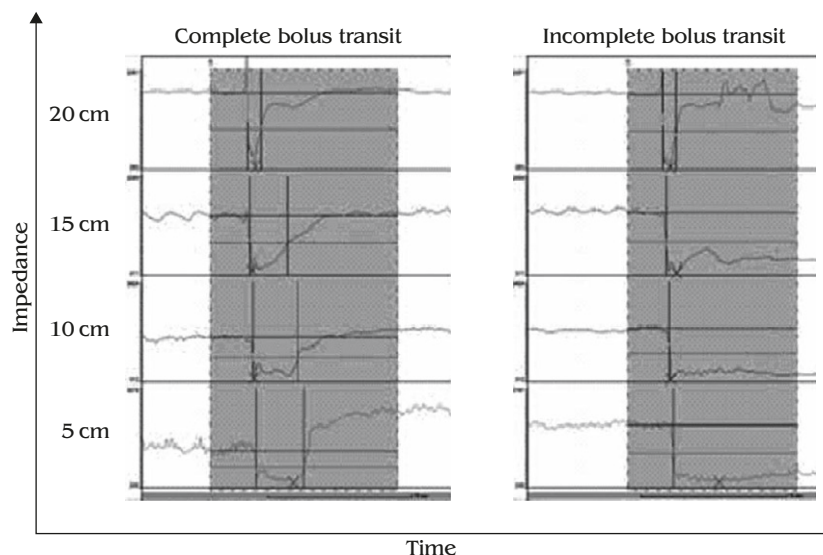


Fig. 5 — Example of impedance tracings of complete and incomplete bolus transit [13].

with liquid and viscous or semisolid boluses. Nguyen et al reported on the dynamics of esophageal bolus transit in 10 healthy subjects who received liquid boluses in the supine and upright positions and semisolid boluses in the supine position (3). Their analysis focused predominantly on bolus head, body, and tail velocities in the pharynx, proximal, middle, and distal third of the esophagus. It was suggested that bolus propagation velocities decreased from proximally to distally and that upright position and bolus consistency influenced bolus transit patterns. In a similar study, the role of gravity and bolus consistency on esophageal contractions and the bolus transit pattern were studied by evaluating these parameters in 10 healthy volunteers positioned at inclinations of 0, 30, 60, and 90 degrees (4). The authors found that the distal esophageal contraction amplitude and the bolus transit times declined with increasing inclination with an almost perfect negative correlation between the angle of inclination and bolus transit time.

Currently, normal values for combined impedance and manometry swallowing have been reported by three groups. Tutuian and coworkers reported normal data from a multicenter study, in which each subject received 10 liquid and 10 viscous swallows at intervals of 20–30 seconds (5). Swallows were classified by manometry as: (1) *normal peristaltic* (defined as contraction amplitudes at both 5 cm and 10 cm above the LES of at least 30 mmHg and onset velocity in the distal esophagus not greater than 8 cm/s); (2) *simultaneous* (defined as contraction with an onset velocity greater than 8 cm/s or retrograde onset and an amplitude >30 mmHg at both 5 cm and 10 cm above the LES); and (3) *ineffective* (defined as contraction amplitude in the distal part of the esophagus less than 30 mmHg). Swallows were classified by impedance

monitoring as having either (a) *CBT* (defined as detection of bolus exit in all three distal impedance channels located at 15 cm, 10 cm, and 5 cm above the LES) or (b) *incomplete bolus transit* (defined as bolus retention in at least one of the three distal impedance channels). Using these definitions, more than 93% of normal individuals were found to have at least 80% of swallows with complete bolus liquid transit or at least 70% of swallows with complete viscous bolus transit.

In another study of 42 healthy volunteers, similar results were found (17) with combined water-perfused manometry-impedance catheters. The authors proposed a more liberal definition of normal bolus clearance, namely, complete bolus clearances of at least 70% of liquid swallows and at least 60% of viscous swallows. The other set of normal data of combined impedance-manometry testing was reported by Nguyen et al in a group of 25 healthy subjects (18). They also reported on normal value of the esophageal baseline impedance and deglutitive impedance gradient during saline and yogurt swallows.

4.3. Esophageal bolus transit in pathologic conditions

Using the established normal values ($\geq 80\%$ complete liquid bolus transit and $\geq 70\%$ complete viscous bolus transit), esophageal function testing was investigated in a group of 350 patients presenting with various esophageal symptoms and having various manometric findings (19). Abnormal bolus transit was found in all patients with achalasia and scleroderma, proving the principle that impedance can assess bolus transit in patients with severe esophageal motility abnormalities. On the other hand, almost all (i.e., $\geq 95\%$)

patients with normal esophageal manometry, nutcracker esophagus, and isolated LES abnormalities (i.e., hypertensive, hypotensive, and poorly relaxing LES) had normal bolus transit for liquid. In the groups of patients with ineffective esophageal motility and diffuse esophageal spasm, approximately half of the patients had normal bolus transit.

Conchillo et al reported on the results of combined impedance–manometry testing in 40 patients with non-obstructive dysphagia (NOD) (20). In this group of patients, abnormal transit for liquid and/or viscous boluses was found in 35.3% of the patients with normal motility and in 100% of the achalasia patients. It was concluded that the addition of impedance to manometry identifies esophageal function abnormalities in patients with NOD in which manometry would have been normal or unspecific.

A more detailed study in 70 patients with ineffective motility identified that there is no perfect (i.e., highly sensitive and highly specific) manometric cut-off that would predict CBT and that the current manometric criteria for diagnosing ineffective motility (i.e., $\geq 30\%$ manometric ineffective swallows) is too sensitive and lacks the specificity of identifying patients with abnormal bolus transit (8). Normal bolus transit in this patient group was likely to be dependent on the distal esophageal contraction amplitude (i.e., average amplitude at the esophageal sites 5 cm and 10 cm above the LES), the number of sites with low contraction amplitudes, and the overall number of manometrically ineffective swallows. Another important finding was that while approximately one third of their patients had normal bolus transit for liquid and viscous swallows (suggesting a mild functional defect), another approximately one third had abnormal bolus transit for either liquid or viscous swallows (i.e., moderate functional defect), and the remaining third had abnormal bolus transit for both liquid and viscous (i.e., severe functional defect).

Although fluoroscopy has the disadvantage of exposing the patient to ionizing radiation, it provides both functional and anatomical information, while with impedance monitoring only functional information is attained. Furthermore, swallows of solid material can be studied fluoroscopically, which is not possible with impedance monitoring. Impedance monitoring does not seem to be very useful for the diagnosis of achalasia and for the follow-up evaluation of esophageal emptying in achalasia patients. Because 100% of the manometrically diagnosed achalasia patients have an abnormal emptying pattern during esophageal function testing and no achalasia-specific impedance abnormalities have yet been reported, impedance monitoring does not contribute to the diagnosis of achalasia (20), and the value of impedance monitoring for assessment of esophageal emptying in achalasia patients appears to be limited.

In summary, current data support the concept that combined impedance monitoring and manometry can be used in research and clinical settings to provide more detailed information on esophageal function. The next step in evaluating the clinical utility of the additional information provided by impedance monitoring is using this technique in clinical conditions such as disordered swallowing or dysphagia, and in interventional outcome studies. These studies would allow a critical evaluation of the proposed parameters and allow quantification of the predictive value of the information provided by impedance measurements.

4.4. Impaired bolus clearance in patients with gastroesophageal reflux disease (GERD)

As shown in our previous work (21), impedance can provide physiologically and clinically relevant information in reflux patients with potentially esophageal dysmotility in whom traditional manometry could provide less definite results. Our findings were similar to a previous study which showed that, in GERD patients, these motor abnormalities lead to substantial impairments in esophageal clearance (22). We found that whereas manometry identified motility abnormalities in approximately one fourth of GERD patients, impedance found that the majority of these patients, as well as some additional patients in whom the manometry results appeared normal, had defective bolus clearance. The fact that none of our asymptomatic subjects had abnormal bolus clearance strongly suggests that the abnormalities we found appear to be highly specific to GERD patients. The ultimate significance of this relatively high prevalence of defective clearance in the pathogenesis of dysphagia or GERD remains to be determined. However, this notion might be partially relevant to the fact that disruption of esophageal peristalsis affects both volume clearance (12) and delivery of swallowed saliva to the distal esophageal body. The other abnormality found in patients with mild esophagitis was an increased basal impedance gradient (23). This finding suggests that persistence of bolus residues in the distal esophagus might be a consequence of impaired distal esophageal motility and underlying prolonged acid clearance.

5. Clinical relevance for impedance monitoring

According to the discussion earlier in this chapter, combined impedance and manometry can be applicable and particularly suitable for physiological investigations of esophageal motor function as well as bolus transport patterns. Therefore, different aspects

of esophageal bolus transport can be obtained: (1) normal and pathological bolus transport patterns including bolus escape and retrograde bolus transport can be monitored; (2) several parameters of bolus transit can be calculated allowing differentiation between normal and abnormal bolus transport; (3) parameters related to bolus clearance and bolus transit completion can be determined; and (4) swallow-associated events such as normal and pathological air movement as well as pathological reflux can be monitored. Thus, detailed information regarding esophageal motor function and associated bolus transport can be obtained by combined impedance and manometry during a single investigation.

In patients with suspected esophageal motor disorder, the technique provides additional information about the functional status of the esophagus and may explain some symptoms in these patients. However, the gold standard for diagnosis of achalasia remains manometry due to its diagnostic criteria and the unique manometry patterns. In patients with reflux disease, combined impedance and manometry may provide additional information about mechanisms related to impaired bolus transit and bolus clearance. In patients with ineffective esophageal motility, it helps clarify the associated functional abnormalities (8). Therefore, combined impedance and manometry is emerging as an important tool for obtaining detailed information about the physiology and pathophysiology of esophageal motility. The future clinical implications of this technique may include: (1) the functional classification of esophageal motor disturbances in patients with NOD; (2) the perioperative management of laparoscopic fundoplication and other endoscopic procedures which could impact esophageal motility; and (3) the physiological characteristics of esophageal bolus transport caused by esophageal stimulation such as secondary peristalsis.

6. Conclusions

In conclusion, intraluminal impedance monitoring has been demonstrated to be a useful tool to investigate esophageal transit in health and disease. This new technique has already been accepted as a valuable instrument in the field of esophageal motility testing for daily gastroenterological practice. However, further studies with properly designed outcomes will be needed before the recommendation by evidence-based medicine can be made.

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